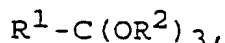


CLAIMS

1✓ A process for the resolution of enantiomeric mixtures of a chiral carboxylic acid of formula



wherein R is a hydrocarbon residue optionally containing one or more heteroatoms and optionally mono- or polysubstituted, comprising an esterification reaction of said carboxylic acid in an organic solvent, in the presence of a stereoselective hydrolase, characterized in that an orthoester of formula



in which  $R^1$  is selected from H and  $C_1-C_4$ alkyl and  $R^2$  is  $C_1-C_8$ alkyl or  $-CH_2-C_6-10$ aryl,

is used as the esterification reactive.

2. A process as claimed in claim 1, wherein  $R^1$  is selected from H, methyl, ethyl, n-propyl, n-butyl.

3. A process as claimed in claim 2, wherein said stereoselective hydrolase is a lipase selected from Candida antarctica, Candida cylindracea, Pseudomonas cepacia, Mucor miehei, Mucor javanicus, Aspergillus niger, swine pancreas, or a protease from Aspergillus subtilis.

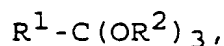
4. A process as claimed in any one of the above claims, wherein said esterification reaction is carried out at a temperature of 0-50°C, preferably at 45°C.

5. A process as claimed in any one of the above claims comprising the step of adding the reaction mixture with an amount of water or of an alcohol with 1-8 carbon atoms equivalent to 1-5% mols compared with the mols of said chiral carboxylic acid.

6. A process as claimed in any one of the above claims, wherein in said esterification reaction the meso form of a bicarboxylic acid is used as substrate.

7. A process as claimed in the above claims 1-6, wherein said carboxylic acid is selected from  $(\pm)$ -(R,S)-2-(2-fluoro-4-biphenyl)-propionic,  $(\pm)$ -(R,S)-2-(3-benzoylphenyl)-propionic,  $(\pm)$ -(R,S)-2-(4-isobutylphenyl)-propionic,  $(\pm)$ -(R,S)-2-[4-(1-oxo-2-isoindolinyl)phenyl]propionic,  $(\pm)$ -(R,S)-2-[4-(2-thenoyl)phenyl]-propionic,  $(\pm)$ -(R,S)-2-(6-methoxy-2-naphthyl)-propionic acids.

8. The use of an orthoester of formula



10 in which  $R^1$  is selected from H and  $C_1-C_4$ alkyl and  $R^2$  is  $C_1-C_8$ alkyl or  $-CH_2-C_6-10$ aryl, in combination with a stereoselective hydrolase in the resolution of enantiomeric mixtures of carboxylic chiral acids.

15 9. The use as claimed in claim 8, wherein said hydrolase is a lipase selected from Candida antarctica, Candida cylindracea, Pseudomonas cepacia, Mucor miehei, Mucor javanicus, Aspergillus niger, swine pancreas, or a protease from Aspergillus subtilis.